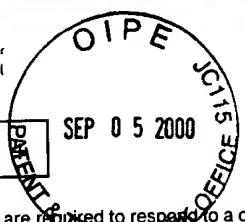


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	<b>Filing Date</b>	06/20/00
	<b>First Named Inventor</b>	A. K. HOPPER
	<b>Group Art Unit</b>	
	<b>Examiner Name</b>	

PH2

<b>Total Number of Pages in This Submission</b>	560	<b>Attorney Docket Number</b>	99-2085
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Anita K. Hopper

Serial No.: 09/599,662

Filed: 06/20/00

Entitled:

Group No.:

Examiner:

**Compositions and Methods for the  
Quantification of Sterol Biosynthetic Flux**

**INFORMATION DISCLOSURE STATEMENT**

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The citations listed below, copies attached, may be material to the examination of the above-identified application, and are therefore submitted in compliance with the duty of disclosure defined in 37 C.F.R. §§ 1.56 and 1.97. The Examiner is requested to make these citations of official record in this application.

The following printed publications are referred to in the body of the specification:

- Arts, *et al.*, "Identification of a nuclear export receptor for tRNA" *Curr Biol* 8:305-314, 1998;
- Bach, "Some new aspects of isoprenoid biosynthesis in plants - A review" *Lipids* 30:191-202, 1995;
- Bartz, *et al.*, "N6-(Delta 2-isopentenyl)adenosine: biosynthesis in vitro in transfer RNA by an enzyme purified from *Escherichia coli*" *Biochem Biophys Res Commun* 40:1481-1487, 1970;

- Benko, *et al.*, "Competition between a sterol biosynthetic enzyme and the tRNA modification in addition to changes in the protein synthesis machinery causes altered nonsense suppression" *PNAS* 97:61-66, 2000;
- Boguta, *et al.*, "Subcellular locations of MOD5 proteins: mapping of sequences sufficient for targeting to mitochondria and demonstration that mitochondrial and nuclear isoforms commingle in the cytosol" *Mol Cell Biol* 14:2298-2306, 1994;
- Brown, *et al.*, "Regression of coronary artery disease as a result of intensive lipid-lowering therapy in men with high levels of apolipoprotein B" *N Engl J Med* 323:1289-98, 1990;
- Brown and Goldstein, "Multivalent feedback regulation of HMG CoA reductase, a control mechanism coordinating isoprenoid synthesis and cell growth" *J Lipid Res.* 21:505-517, 1980;
- Carlson and Botstein, *et al.*, "Two differentially regulated mRNAs with different 5' ends encode secreted with intracellular forms of yeast invertase" *Cell* 28:145-154, 1982;
- Chen, *et al.*, "PPQ, a novel protein phosphatase containing a Ser<sup>+</sup> Asn-rich amino-terminal domain, is involved in the regulation of protein synthesis" *Eur J Biochem* 218:689-699, 1993;
- Chijiwa and Linscheer's (Chijiwa and Linscheer, "Effect of intraluminal pH on cholesterol and oleic acid absorption from micellar solutions in rat" *Am J Physiol* 246:G492-G499, 1984;
- Current Protocols in Immunology (1998) John Wiley and Sons, Inc., N.Y.<sup>1</sup>
- Current Protocols in Molecular Biology (1996) John Wiley and Sons, Inc., N.Y.<sup>2</sup>;

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<sup>1</sup> This reference is not included. This is a general text book and was cited in the spec without any reference to specific pages.

<sup>2</sup> This reference is not included. This is a general text book and was cited in the spec without any reference to specific pages.

- Dihanich, *et al.*, "Isolation and characterization of MOD5, a gene required for isopentenylation of cytoplasmic and mitochondrial tRNAs of *Saccharomyces cerevisiae*" *Mol Cell Biol* 7:177-184, 1987;
- Donald, *et al.*, "Effects of overproduction of the catalytic domain of 3-hydroxy-3-methylglutaryl coenzyme A reductase on squalene synthesis in *Saccharomyces cerevisiae*" *Appl Environ Microbiol* 63:3341-3344, 1997;
- Endo, *et al.*, "Beneficial effects of dietary intervention on serum lipid and apolipoprotein levels in obese children" *Am J Dis Child* 146:303-305, 1992;
- Endo, *et al.*, "Oxygenated cholesterol as ligands for cytosolic-nuclear tumor promoter binding protein: yakasteroids" *Biochem Biophys Res Commun* 194:1529-35, 1993;
- Endo, "The discovery and development of HMG-CoA reductase inhibitors" *J Lipid Res* 33:1569-1582, 1992
- Endres *et al.*, "Role of peroxynitrite and neuronal nitric oxide synthase in the activation of poly(ADP-ribose) synthetase in a murine model of cerebral ischemia-reperfusion" *Neurosci Lett.* 248:41-41, 1998;
- Frantz and Gilbert, "A novel yeast gene product, G4p1, with a specific affinity for quadruplex nucleic acids" *J Biol Chem* 270:20692-20697, 1995;
- Gibbs and Oliff, "The potential of farnesyltransferase inhibitors as cancer chemotherapeutics" *Annu Rev Pharmacol Toxicol.* 37:143-66, 1997;
- Gietz, *et al.*, "Improved method for high efficiency transformation of intact yeast cells" *Nucleic Acids Res* 20:1425, 1992;
- Gillman, *et al.*, "MOD5 translation initiation sites determine N6-isopentenyladenosine modification of mitochondrial and cytoplasmic tRNA" *Mol Cell Biol* 11:2382-2390, 1991;
- Goldstein and Brown, "Regulation of the mevalonate pathway" *Nature* 343:425-430, 1990;
- Hinnebusch and Liebman, in The molecular and cellular biology of the yeast *Saccharomyces*: Genomic dynamics, protein synthesis and energetics eds. Broach, *et al.* "Protein Synthesis and Translational Control in *Saccharomyces*

*cerevisiae*" [Cold Spring Harbor Lab Press, Plainview, NY] Vol. 1, pp. 627-735, 1991;

- Hopper, *et al.*, "Processing of intervening sequences: a new yeast mutant which fails to excise intervening sequences from precursor tRNAs" *Cell* 19:741-751, 1980;
- Janssen and Möller, "Elongation factor 1  $\beta$   $\gamma$  from *Artemia*. Purification and properties of its subunits" *Eur J Biochem* 171:119-129, 1988;
- Kinzy, *et al.*, "Multiple genes encode the translation elongation factor EF-1 $\gamma$  in *Saccharomyces cerevisiae*" *Nucleic Acids Res* 22:2703-2707, 1994;
- Kline, *et al.*, "N<sup>6</sup>-( $\Delta^2$ -Isopentenyl) adenosine. Biosynthesis in transfer ribonucleic acid *in vitro*" *Biochemistry* 8:4361-4371, 1969;
- Laten, *et al.*, "Isopentenyladenosine deficient tRNA from an antisuppressor mutant of *Saccharomyces cerevisiae*" *Nucleic Acids Res* 5:4329-4342, 1978;
- Laufs *et al.*, "Upregulation of endothelial nitric oxide synthase by HMG CoA reductase inhibitors" *Circulation* 97:1129-35, 1998;
- Liu, *et al.*, "Construction of a GAL1-regulated yeast cDNA expression library and its application to the identification of genes whose overexpression causes lethality in yeast" *Genetics* 132:665-673, 1992;
- Lund and Dahlberg, "Proofreading and aminoacylation of tRNAs before export from the nucleus" *Science* 282:2082-2085, 1998;
- Martin and Hopper, "Isopentenylation of both cytoplasmic and mitochondrial tRNA is affected by a single nuclear mutation" *J Biol Chem* 257:10562-10565, 1982;
- McCloskey and Nishimuta, "Modified Nucleosides in Transfer RNA" *Acc. Chem. Res.* 10:403-410, 1977;
- McKnight *et al.*, "Selection of Functional cDNAs by complementation in yeast," *PNAS* 80:4412-4416, 1983;
- Najarian *et al.*, "DNA Sequence and Transcript Mapping of MOD5: Features of the s' Region which Suggest Two Translational Starts," *Mol. Cell. Biol.* 7:185-191, 1987

- Nash, "Meeting National Cholesterol Education Goals in Clinical Practice-A Comparison of Lovastatin and Fluvastatin in Primary Prevention," *Am J. Cardiol.* 78(Suppl. 6A):26:31, 1996
- Nasmyth and Tatchell, "The structure of transposable yeast mating type loci" *Cell* 19:753-764, 1980
- Ono *et al.*, "Nonsense Mutations in the can1 Locus of *Saccharomyces cerevisiae*," *J. Bacteriology* 154:1476-1479, 1983;
- Rasmussen and Culbertson, "Analysis of yeast trimethylguanosine-capped RNAs by Midwestern blotting" *Gene* 182:89-96, 1996;
- Rasse-Messenguy and Fink, "Temperature-sensitive nonsense suppressors in yeast" *Genetics* 75:459-464, 1973;
- Rine, "Gene overexpression in studies of *Saccharomyces cerevisiae*" *Methods Enzymol* 194:239-251, 1991;
- Rosenbaum and Gefter, " $\Delta^2$ -Isopentenylpyrophosphate: Transfer Ribonucleic Acid  $\Delta^2$ -Isopentenyltransferase from *Escherichia coli*. Purification and properties of the enzyme" *J Biol Chem* 247:5675-5680, 1972;
- Rothstein, "Targeting, disruption, replacement, and allele rescue: integrative DNA transformation in yeast" *Methods Enzymol* 194:281-301, 1991;
- Sambrook *et al.* *Molecular Cloning: A Laboratory Manual*, 2d ed. (1989) Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., and *Current Protocols in Molecular Biology* (1996) John Wiley and Sons, Inc., N.Y.<sup>3</sup>;
- Sanger, *et al.*, "DNA sequencing with chain-terminating inhibitors" *Proc Natl Acad Sci USA* 74:5463-5467, 1977;
- Sarkar, *et al.*, "Nuclear tRNA aminoacylation and its role in nuclear export of endogenous tRNAs in *Saccharomyces cerevisiae*" *PNAS* 96:14366-14371, 1999;
- Sarkar and Hopper, "tRNA nuclear export in *Saccharomyces cerevisiae*: in situ hybridization analysis" *Mol Biol Cell* 9:3041-3055, 1998;

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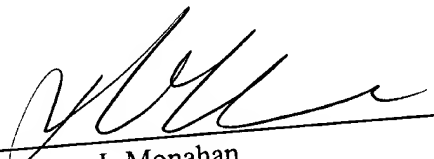
<sup>3</sup> This reference is not included. This is a general text book and was cited in the spec without any reference to specific pages.

- Senapathy and Jacob, "Identification and purification of tRNAs containing N6-(delta 2-isopentenyl) adenosine using antibodies specific for N6-(delta-isopentenyl) adenosine" *J Biol Chem* 256:11580-11584, 1981;
- Simos, *et al.*, "The yeast protein Arc1p binds to tRNA and functions as a cofactor for the methionyl- and glutamyl-tRNA synthetases" *EMBO J* 15:5437-5448, 1996;
- Sinensky, *et al.*, "Differntail inhibitory effects of lovostatin on protein isoprenylation and sterol synthesis" *J Biol Chem* 265:19937-19941, 1990;
- Sinha *et al.*, "Polymer support oligonucleotide synthesis XVIII1.2:use of  $\beta$ -cyanoethyl-N, N-dialkylamino-/N-morpholono phosphoramidite of deoxynucleosides for the synthesis of DNA fragments simplifying deprotection and isolation of the final product," *Nucleic Acids Res.* 12:4539-4557, 1984;
- Song, *et al.*, "Elongation factor EF-1 alpha gene dosage alters translational fidelity in *Saccharomyces cerevisiae*" *Mol Cell Biol* 9:4571-4575, 1989;
- Stansfield, *et al.*, "The products of the SUP45 (eRF1) and SUP35 genes interact to mediate translation termination in *Saccharomyces cerevisiae*" *EMBO J* 14:4365-4373, 1995;
- Stansfield and Tuite, "Polypeptide chain termination in *Saccharomyces cerevisiae*" *Curr Genet* 25:385-395, 1994;
- Tanimoto *et al.*, "Inhibitory activity to protein prenylation and antifungal activity of zaragozic acid D3, a potent inhibitor of squalene synthase produced by the fungus, *Mollisia* sp SANK 10294" *J Antibiot (Tokyo)* 51:428-431, 1998;
- Vincent, *et al.*, "The yeast translational allosuppressor, SAL6: a new member of the PP1-like phosphatase family with a long serine-rich N-terminal extension" *Genetics* 138:597-608, 1994;
- Voet and Voet, in Biochemistry "Lipid Metabolism," John Wiley & Sons, Inc. Chapter 23 pp.645-657, 1990;
- Ward, "Single-step purification of shuttle vectors from yeast for high frequency back-transformation into *E.coli*" *Nucleic Acids Res* 18:5319, 1990;
- Whelan *et al.*, "The *CAN1* locus of *Saccharomyces cerevisiae*: fine-structure analysis and forward mutation rates" *Genetics* 91:35-51, 1979;

- Woolford and Warner, in The molecular and cellular biology of the yeast *Saccharomyces*: Genomic dynamics, protein synthesis and energetics eds. Broach, *et al.* "The Ribosome and Its Synthesis" [Cold Spring Harbor Lab Press, Plainview, NY] Vol. 1, pp. 587-626, 1991; and
- Zoladek *et al.*, "Mutations altering the mitochondrial-cytoplasmic distribution of Mod5p implicate the actin cytoskeleton and mRNA 3' ends and/or protein synthesis in mitochondrial delivery" *Mol Cell Biol.* 15:6884-6894, 1995.

This Information Disclosure Statement under 37 C.F.R. §§ 1.56 and 1.97 is not to be construed as a representation that a search has been made, that additional information material to the examination of this application does not exist, or that any one or more of these citations constitutes prior art.

Dated: August 31, 2000

  
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